Brief Report: Immune Microenvironment Determines the Immunogenicity of Induced Pluripotent Stem Cell Derivatives.

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Authors: Dilyana Todorova, Jinchul Kim, Sara Hamzeinejad, Jingjin He, Yang Xu

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Public Summary:
The breakthrough of induced pluripotent stem cells (iPSCs) has raised the possibility that patient-specific iPSCs can provide autologous cells for cell therapy without the concern for immune rejection. However, the immunogenicity of iPSC-derived cells remains controversial. Using syngeneic C57BL/6 (B6) mouse transplantation model, several studies indicate that B6 iPSC-derived cells exhibit some levels of immunogenicity when transplanted into B6 mice subcutaneously. In contrast, one recent study has concluded that various lineages of B6 iPSC-derived cells exhibit no immunogenicity when transplanted under the kidney capsule of B6 mice. To resolve the controversy concerning this critical issue of iPSC biology, we used the same B6 transplantation model to demonstrate that the immune response toward antigens is dependent on the immune environment of the transplantation site. Immunogenic antigen-expressing B6 embryonic stem cells (ESCs) as well as B6 iPSCs and their terminally differentiated cells survived under the kidney capsule but are immune rejected when transplanted subcutaneously or intramuscularly. The cotransplantation of mature B6 dendritic cells under the kidney capsule leads to immune rejection of B6 iPSC-derived grafts but not B6 ESC-derived grafts, indicating that the lack of detectable immune response to iPSC-derived grafts under the kidney capsule is due to the lack of functional antigen presenting cells.

Scientific Abstract:
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